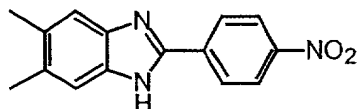
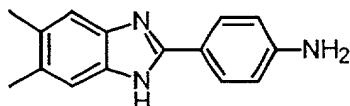


[0059] 2-(4-Aminophenyl)-5,6-dimethyl benzimidazole was synthesized from 2-(4-nitrophenyl)-5,6-dimethyl benzimidazole, which was prepared by mixing 1,2-diamino-4,5-dimethylbenzene (1.38 g, 10.1 mmole) with 4-nitrobenzoic acid (1.69 g, 9.9 mmole) and dissolved in POCl_3 (10 ml) and heated to reflux for 2.5 hours. The reaction mixture was cooled and cautiously poured onto ice. The resulting solid was filtered, washed with NaHCO_3 and used without further purification.



2-(4-nitrophenyl)-5,6-dimethyl benzimidazole

[0060] 2-(4-Aminophenyl)-5,6-dimethyl benzimidazole was synthesized by dissolving 1 g of the above nitrobenzimidazole (31.1) in 30% $\text{Na}_2\text{S} \cdot 9\text{H}_2\text{O}$ (20 ml) with stirring at RT for 4.5 h. The reaction mixture was diluted with water and extracted with EtOAc. The combined organic extracts were dried over sodium sulfate and concentrated under vacuum. The product was characterized by mass spectroscopy.



2-(4-aminophenyl)-5,6-dimethyl benzimidazole

[0061] The subsequent preparation of symmetrical diamides was accomplished by one of the following methods:

[0062] Method A: 2-(4-Aminophenyl)-6-aminobenzimidazole (1 mmole) was suspended in THF (5 ml) to which was added DIEA (2.5 mmole) and mixture cooled to -78°C . To the above cooled mixture was added the acid chloride (2.5 mmole) and let warm to RT overnight. Water (2 ml) is added to the reaction and extracted with EtOAc. The combined organic extracts were combined washed with NaHCO_3 (aq.) and concentrated under reduced pressure. The resulting residue was purified on silica gel (hexanes/EtOAc or $\text{MeOH}/\text{CH}_2\text{Cl}_2$) or reverse phase HPLC ($\text{CH}_3\text{CN}/\text{H}_2\text{O}$).

[0063] Method B: 2-(4-Aminophenyl)-6-aminobenzimidazole (1 mmole) and DMAP (cat.) was dissolved in pyridine (5 ml). To the above solution was added the acid chloride (2.5 mmole) and the reaction stirred overnight at 60° C. The reaction was cooled to room temperature and water added to precipitate the product. The resulting solid was collected by filtration with the solid being washed by hexanes and water and NaHCO₃ (aq.). The resulting residue was purified on silica gel (hexanes/EtOAc or MeOH/CH₂Cl₂) or reverse phase HPLC (CH₃CN/H₂O).

[0064] Method C: 2-(4-Aminophenyl)-6-aminobenzimidazole (1 mmole) was suspended in THF (10 ml) to which was added K₂CO₃ (2.5 mmole) in water (0.5 ml). and mixture cooled to -78° C. To the above cooled mixture was added the acid chloride (2.5 mmole) and let warm to RT overnight. Water (10 ml) was added to the reaction and extracted with EtOAc. The combined organic extracts were combined washed with NaHCO₃ (aq.) and concentrated under reduced pressure. The resulting residue was purified on silica gel (hexanes/EtOAc or MeOH/CH₂Cl₂) or reverse phase HPLC (CH₃CN/H₂O).

[0065] Method D: The carboxylic acid (2.2 mmole), EDC (2.2 mmole) and DMAP (cat.) was dissolved in hot pyridine. To the above solution was added 2-(4-aminophenyl)-6-aminobenzimidazole (1 mmole) and heated to 60° C overnight. The cooled reaction mixture was partitioned between water and EtOAc. The organic layer was washed with NaHCO₃, dried over Na₂SO₄ and concentrated under vacuum. The resulting residue was purified on silica gel (hexanes/EtOAc or MeOH/CH₂Cl₂) or reverse phase HPLC (CH₃CN/H₂O).

Benzimidazole Species

[0066] The following species encompassed within the disclosed generic formula were synthesized and tested for their ability to suppress IgE. The species are presented below.

